IFW

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,367	10/24/2003	Audrey Minden	0575/55311-AZ-PCT-US	2322

7590 04/17/2006

John P. White, Esq.
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/693,367	MINDEN, AUDREY	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65,67 and 68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65,67 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 9, 2006 has been entered.

Applicant's response and amendments received February 9, 2006 are acknowledged.

Claims 1-64 and 66, and 69-71 are canceled.

Claim 65 has been amended.

Claims 65, 67, and 68 are pending and under consideration in this Office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65, 67, and 68 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention for the reasons made of record in the Office action mailed October 18, 2004.

Applicant's arguments filed February 9, 2006 have been fully considered but they are not persuasive.

Claims 65, 67 and 68 were rejected previously as lacking adequate written description under 35 U.S.C. 112, first paragraph because the breadth of applicant's claims originally read upon antibodies that bound all mammalian PAK4 kinases, as well as allelic variants, analogs, fragments, or derivatives of mammalian PAK4 kinases. The disclosure provided by applicant contains an 89 amino acid partial sequence of mouse PAK4 (SEQ ID NO: 14), the full-length sequence of human PAK4 (SEQ ID NO: 2), a deletion mutant that lacks the GTPase binding domain, and the human point mutants K(350)M, S(474)M and S(474)E. Applicant's amendment of base claim 65 received February 9, 2006 recites "A purified antibody capable of specifically binding to a human PAK4 serine/threonine kinase comprising the GTPase binding domain contained within residues 10-30 of the amino acid sequence set forth in SEQ ID NO:2." Applicant argues on page 6 of the reply received February 9, 2006 that the scope of the claim is now limited to an antibody that binds a human PAK4 that has the GTPase binding domain

but does not bind to human PAK4 that lacks the recited domain and that the recited antibody does not bind to allelic variants, fragments, or derivatives of PAK4. The examiner disagrees with applicant as to the actual scope of the claimed invention.

Claim 65 as amended indicates that the claimed antibody must be capable of binding a human PAK4 molecule that comprises the recited domain. The claim does not indicate that the claimed antibody binds to PAK4 within this domain, only that a protein bound by the antibody comprises this domain. As such the true scope of the claim encompasses antibodies that bind to any epitope found within any PAK4 allelic variant, fragment, derivative or other form of PAK4 that comprises the recited sequence. Thus the claimed invention still reads on antibodies that bind allelic variants, fragments derivatives and other forms of PAK4. Note that limitations added by dependent claims 67 and 68 do not address this issue.

The specification does not define human PAK4 as being limited to SEQ ID NO:2, and indeed PAK4 molecules that differ from the disclosed sequences are disclosed as being part of the invention (see particularly page 13, lines 20-37, page 14, lines 13-38 and page 15, lines 1-16). As indicated above, the only allelic variants, analogs, fragments, or derivatives of PAK4 that appear to be disclosed by applicant in the specification are non-naturally occurring mutant sequences of human PAK4 and a fragment of mouse PAK4. As indicated in the office action mailed October 18, 2004:

"...other than for the already indicated deletion and point mutants, the structure and properties of these PAK4 analogs, fragments, and derivatives are not disclosed, nor is it disclosed how the structures of PAK4 analogs, fragments, and derivatives relate to

their functional properties. As such, the variation in structure and functional properties of such a genus of molecules is substantial." Given that there is substantial variation in PAK4 molecules of the instant application, the variation in the genus of antibodies that bind such molecules is the same or greater.

The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3). As discussed above, the structure and function of the genus of PAK4 molecules that are bound by the claimed antibodies are not disclosed, and further the claimed genus of antibodies has no functional property other than that it binds to a PAK4 polypeptide.

Since there is high variability amongst the genus of antibodies of the claimed invention, and since applicant has disclosed only a limited amount of the genus of molecules bound by said antibodies, the claimed invention does not have written support within the originally filed specification. Thus, applicant was not in possession of the claimed genus antibodies that bind human PAK4 polypeptides which comprise a GTPase binding domain. Applicant is again directed to the Guidelines for the

Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 65, 67 and 68 stand rejected under 35 U.S.C. 102(e) as being anticipated by Plowman et al., U.S. Patent Application Publication No. US 2003/0050230 (of record, see entire document) as evidenced by Goldsby et al. (Immunology, 5th edition, 2002, pages 62-67, of record) and as evidenced by Kuby (Immunology, 1991, page 125) for the reasons of record set forth in the Office action mailed October 18, 2004.

Plowman et al. disclose two polypeptide sequences identified as PAK5, one partial sequence (SEQ ID NO: 30 of Plowman et al., 398 amino acids long) and one full-length sequence (SEQ ID NO: 103 of Plowman et al., 591 amino acids long). The 398 amino acid sequence is 100% identical to SEQ ID NO:2 (571 amino acids long), while SEQ ID NO:2 is 100% identical to the 591 amino acid sequence of Plowman et al.

Plowman et al. also claim an antibody or antibody fragment having specific binding affinity to the kinase polypeptide PAK5 or to a kinase domain peptide of PAK5 (see page 9, paragraphs 63-69, and claim 21 from Plowman et al.). These antibodies to PAK5 can be either monoclonal or polyclonal (see page 9, paragraphs 63-69, and claim 21 from Plowman et al.). The 398 amino acid sequence of Plowman et al., as well as antibodies to said sequence, are fully supported in their provisional application 60/081,784 filed April 14, 1998 (see additionally pages 27-28, paragraphs 350-368).

Applicant's arguments on pages 6-8 of the response filed February 9, 2006 have been fully considered but they are not persuasive. Applicant argues that since the claim recites that the antibody specifically binds a polypeptide comprising residues 10-30 of SEQ ID NO:2, that the art of Plowman et al. cannot anticipate since the sequence now recited in the claims is not disclosed in Plowman et al.'s provisional application.

Applicant is correct that Plowman et al. do not teach a polypeptide that comprises amino acids 10-30 of SEQ ID NO:2. It should be noted that the claimed invention is an antibody that binds a polypeptide which comprises amino acids 10-30 of SEQ ID NO:2, and is not the polypeptide of SEQ ID NO:2 or a polypeptide which comprises amino acids 10-30 of SEQ ID NO:2. The claims recite that the antibody binds any polypeptide which comprises amino acids 10-30 of SEQ ID NO:2, but the claims do not recite that the epitope which the claimed antibody binds within this genus of polypeptides that includes SEQ ID NO:2 (i.e. the claimed antibody can bind anywhere within SEQ ID NO:2, not just the epitope of amino acids 10-30 of SEQ ID NO:2, and further can bind any epitope of any sequence so long as said sequence is present in a

polypeptide, such as but not limited to fusion proteins, which comprise the GTPase binding domain of amino acids 10-30 of SEQ ID NO:2). As has been indicated repeatedly through prosecution, antibodies that bind epitopes within the 398 amino acid sequence disclosed by Plowman et al. would also bind SEQ ID NO:2 (which necessarily comprises amino acids 10-30 of SEQ ID NO:2) since SEQ ID NO:2 comprises the 398 amino acid sequence of Plowman et al. Antibodies bind to epitopes and not to whole proteins. Typically, between 15-22 amino acids of a protein antigen are bound by an antibody molecule (see Goldsby et al., pages 62-67, particularly page 63, the second full paragraph of the left column, of record). Therefore, there are many shared epitopes between the 398 amino acid sequence of Plowman et al. and SEQ ID NO:2 of the instant invention. Since the structures (i.e. the amino acid sequences) of these epitopes are identical, an antibody generated against such an epitope would necessarily bind both sequences. The phenomenon by which antibodies bind the same epitope within a different polypeptide is known in the art as cross-reactivity (Kuby, J. Immunology, 1991, see page 125, particularly the first two sentences of the first full paragraph of the page). Applicant has repeated the prior argument that the recitation of "specifically binding" would indicate to one skilled in the art that the claimed antibody binds to a polypeptide that comprises amino acids 10-30 of SEQ ID NO:2 but would not bind to a polypeptide that lacks amino acids 10-30 of SEQ ID NO:2 (for example, see the first full sentence of page 6 of applicant's reply received February 9, 2006). As such, applicant argues that the recitation of "specifically binding" excludes the art-recognized phenomenon of cross-reactivity discussed above. The specification does not appear to support applicant's

use of the phrase "specifically binding" such that it excludes cross-reactivity. As such, this recitation and the language of the claims as amended February 9, 2006 fail to distinguish the claimed invention from that disclosed and claimed by Plowman et al. and the rejection of record is maintained.

Therefore, the prior art anticipates the claimed invention.

5. No claims are allowable.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
April 4, 2006

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600

Notice of References Cited	Application/Control No. 10/693,367	Applicant(s)/Patent Under Reexamination MINDEN, AUDREY	
	Examiner Michael Szperka	Art Unit 1644	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Kuby, J. Immunology, W. H. Freeman and Company, 1991, page 125.
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

IMMUNOLOGY

Janis Kuby

Professor of Biology,
San Francisco State University

Faculty,
Joint Medical Program,
University of California at Berkeley

W. H. Freeman and Company
New York

Library of Congress Cataloging-in-Publication Data

Kuby, Janis.
Immunology / Janis Kuby.
p. cm.
Includes bibliographical references and index.
ISBN 0-7167-2257-7
1. Immunology. I. Title.
[DNLM: 1. Immune System. 2. Immunity. QW 504 K95i]
QR181.K83 1992
616.07'9—dc20
DNLM/DLC
for Library of Congress

91-44429
CIP

Printed in the United States of America

1 2 3 4 5 6 7 8 9 0 RRD 9 9 8 7 6 5 4 3 2 1 0

teractions seen with biological systems, as in the case of antibody's reaction with determinants on a virus or a bacterial cell. Avidity can compensate for low affinity. For example, secreted pentameric lgM often has a lower affinity than lgG, but because of its high avidity, resulting from its multivalence, it binds effectively to antigen.

Cross-Reactivity

Although the antigen-antibody reaction is highly specific, in some cases antibody elicited by one antigen can cross-react with an unrelated antigen. Such cross-reactions occur if two different antigens share an identical epitope or if antibodies specific for one epitope also bind to an unrelated epitope possessing similar chemical properties. In the latter case the antibody's binding affinity for the cross-reacting epitope is usually less than that for the original epitope.

Cross-reactivity is often observed among polysaccharide antigens that contain similar oligosaccharide residues. The ABO blood-group antigens, for example, are glycoproteins expressed on red blood cells. Subtle differences in the terminal sugar residues distinguish the A and B blood-group antigens. An individual lacking one or both of these antigens will have antibodies to the missing antigen(s). A type O individual thus has anti-A and anti-B antibodies; a type A individual has anti-B; and a type B individual has anti-A. Cross-reactivity is the basis for the presence of these blood-group antibodies, which are induced in an individual not by exposure to red blood cell antigens but by exposure to cross-reacting microbial antigens present on common intestinal bacteria. These cross-reacting microbial antigens induce the formation of antibodies in individuals lacking these antigens. The blood-group antibodies, although elicited by microbial antigens, will cross-react with similar oligosaccharides on red blood cells.

A number of viruses and bacteria possess antigenic determinants identical to or similar to normal host-cell components. In some cases these microbial antigens have been shown to elicit antibody that cross-reacts with the host-cell components, resulting in a tissue-damaging autoimmune reaction. The bacterium *Streptococcus pyogenes* expresses cell-wall proteins called M antigens. Antibodies produced to streptococcal M antigens have been shown to cross-react with several myocardial and skeletal muscle proteins and have been implicated in heart and kidney damage following streptococcal infections. The role of other cross-reacting antigens in the development of autoimmune diseases is discussed in Chapter 17.

Some vaccines also exhibit cross-reactivity. For example, vaccinia virus, which causes cowpox, expresses cross-reacting epitopes with the variola virus, the causative agent of smallpox. This cross-reactivity was the

Table 6-2 Cross-reactivity of three rabbit antialbumin antisera to albumin from various species

	Index of dissimilarity		
Albumin Source	Rabbit antiserum to human albumin	Rabbit antiserum to chimpanzee albumin	Rabbit antiserum to gibbon albumin
Human	1.00	1.09	1.29
Chimpanzee	1.14	1.00	1.40
Gorilla	1.09	1.17	1.31
Orangutang	1.22	1.24	1.29
Siamang	1.30	1.25	1.07
Gibbon	1.28	1.25	1.00
Old World monkeys	2.46	2.22	2.29

* A higher index of dissimilarity indicates less reactivity between specific antibody and an unrelated albumin. The reactivity between each antialbumin antiserum and the albumin used to elicit it is set at 1.00.

SOURCE: V. M. Sarich and A. C. Wilson, 1967, *Science* 158:1200.

Organization TC1600 Bldg./Room REMSEN

U. S. DEPARTMENT OF COMMERCE
COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
IF UNDELIVERABLE RETURN IN TEN DAYS

OFFICIAL BUSINESS

UNITED STATES POSTAGE
02 1A
0004205065
MAILED FROM

AN EQUAL OPPORTUNITY EMPLOYER

A C S
☐ INSUFFICIENT ADDRESS
☐ ATTEMPTED NOT KNOWN
☐ NO SUCH NUMBER/ STREET
☒ NOT DELIVERABLE AS ADDRESSED - UNABLE TO FORWARD
☐ OTHER

RTS
RETURN TO SENDER